Please see below for a link to the webinar recording for the Trials Methodology Research Partnership:

Global Health Trials Methodology

Elizabeth Allen, University of Cape Town – South Africa

Arancha De La Horra Gozalo, University of Oxford – UK

Sylivia Nalubega, Soroti University – Uganda

Jamlick Karumbi, KEMRI Wellcome Trust - Kenya

Mercy Chepkirui, KEMRI Wellcome Trust – Kenya

Naomi Waithira, Mahidol Oxford Research Unit - Thailand

19 October 2020

The slides are also available below.

For any queries, please contact uktmn@nottingham.ac.uk

https://www.youtube.com/watch?v=Yf8aP1Eiouw

TMRP Methodology Webinar Series – Global Health Trials Methodology

Monday 19 October 2020

Elizabeth Allen – University of Cape Town, South Africa
Arancha De La Horra Gozalo – University of Oxford, UK
Sylivia Nalubega – Soroti University, Uganda
Jamlick Karumbi – KEMRI-Wellcome Trust, Kenya
Mercy Chepkirui – KEMRI-Wellcome Trust, Kenya
Naomi Waithira – Mahidol University, Thailand

Trials Methodology TMRP Research Partnership

Global Health Working Group

MRC Medical Research Council

NIHR National Institute for Health Research

University of Cape Town · Universiteit van Kaapstad · iYunivesithi yaseKapa

LSTM Liverpool School of Tropical Medicine

University of Oxford

The Global Health Network
Enabling research by sharing knowledge

Trials methodology research

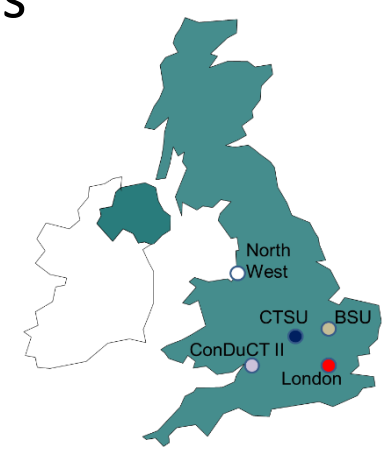
Improving the design, conduct, analysis of trials

- Exploring/comparing methods, generating evidence for & implementing the most effective, appropriate methods
  - Research questions
  - Design (including e.g. outcomes)
  - Planning, conduct (operations, data management)
  - Analysis
  - Reporting/dissemination, secondary use

Ultimately improving patient care

Hubs for Trials Methodology Research

- Promoting high quality collaborative research
- Advice on development of innovative methods
- Strengthening research training & capacity
  - 5 ‘hubs’ in UK academic trial units/groups
  - 9 working groups (topics)
  - 400+ colleagues
  - 50+ funded/partially funded/supported projects
  - 25 PhD students

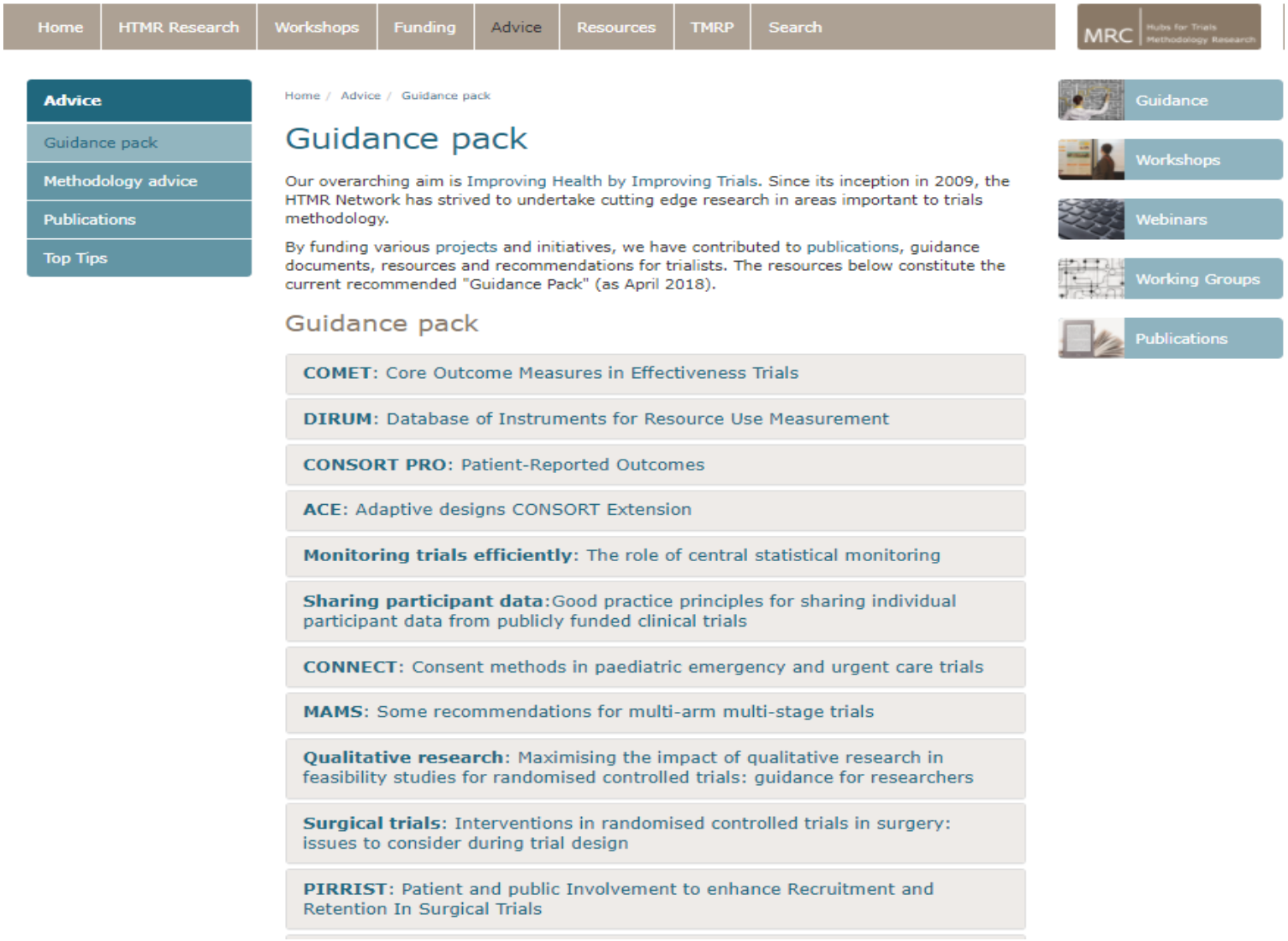


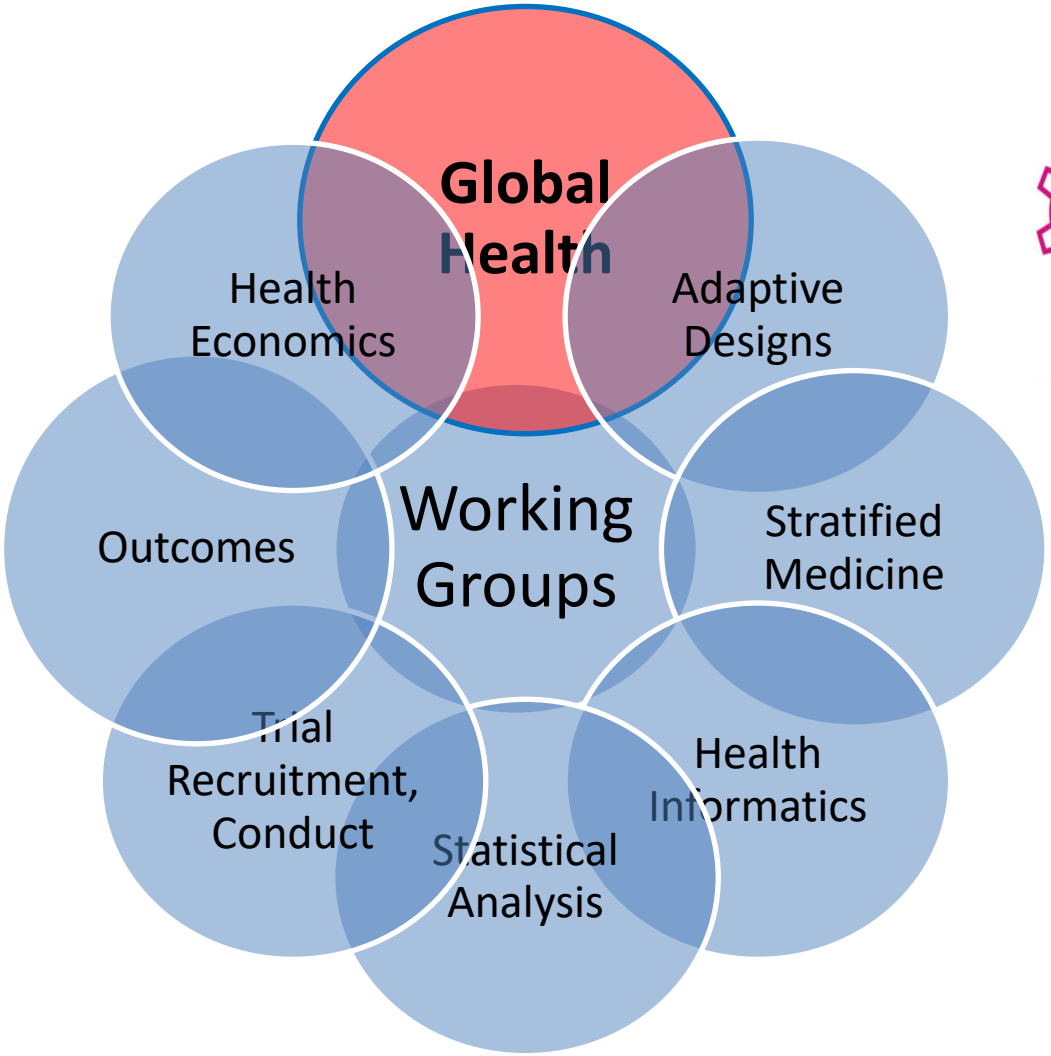
www.methodologyhubs.mrc.ac.uk

MRC | Hubs for Trials Methodology Research

Guidance

www.methodologyhubs.mrc.ac.uk





Trials Methodology TMRP Research Partnership

MRC Hubs for Trials Methodology Research

UKTMN Trial Managers' Network

HDRUK Health Data Research UK

Health Research Board TMRN Trials Methodology Research Network

UKCRC Registered Clinical Trials Units

THE GLOBAL HEALTH NETWORK

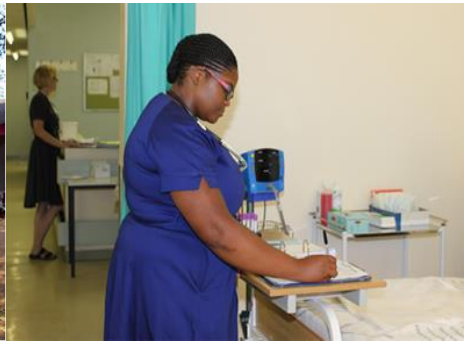
More and better, larger network within & outside of UK

MRC Medical Research Council

NIHR National Institute for Health Research

A global community of practice for Trials Methodology Research

- Trials everywhere benefit from insight & experiences of those working in HICs & LMICs
- Cannot assume a method can be transported into other contexts (e.g. modes of questionnaires)
- Trial staff can & should contribute to finding the best ways of doing their role (extra funding stream……)



Remit of the Global Health WG

- Raise awareness of the field/scope of CTMR in LMICs
- Signpost to other working groups of the TMRP
- Increase capacity though freely accessible resources, training, networking
- Respond to queries from those in LMICs wanting guidance on methods, potential collaborators etc.
- Facilitate small grants for LMICs

Activity thus far

- Eliciting applications for membership (48)
  - All topic areas/can join those WGs too
- Integration with the Global Health Network's Global Heath Methodology Research hub
  - Webinars, newsletters, articles
- Twitter feed (@GHWG_TMRP)
- TGHN competition to win attendance at ICTMC 2019
- First online meeting 5th Nov

https://globalresearchmethods.tghn.org/

www.methodologyhubs.mrc.ac.uk

Pump priming awards

- 270 applications from 48 LMICs
- 7 funded projects

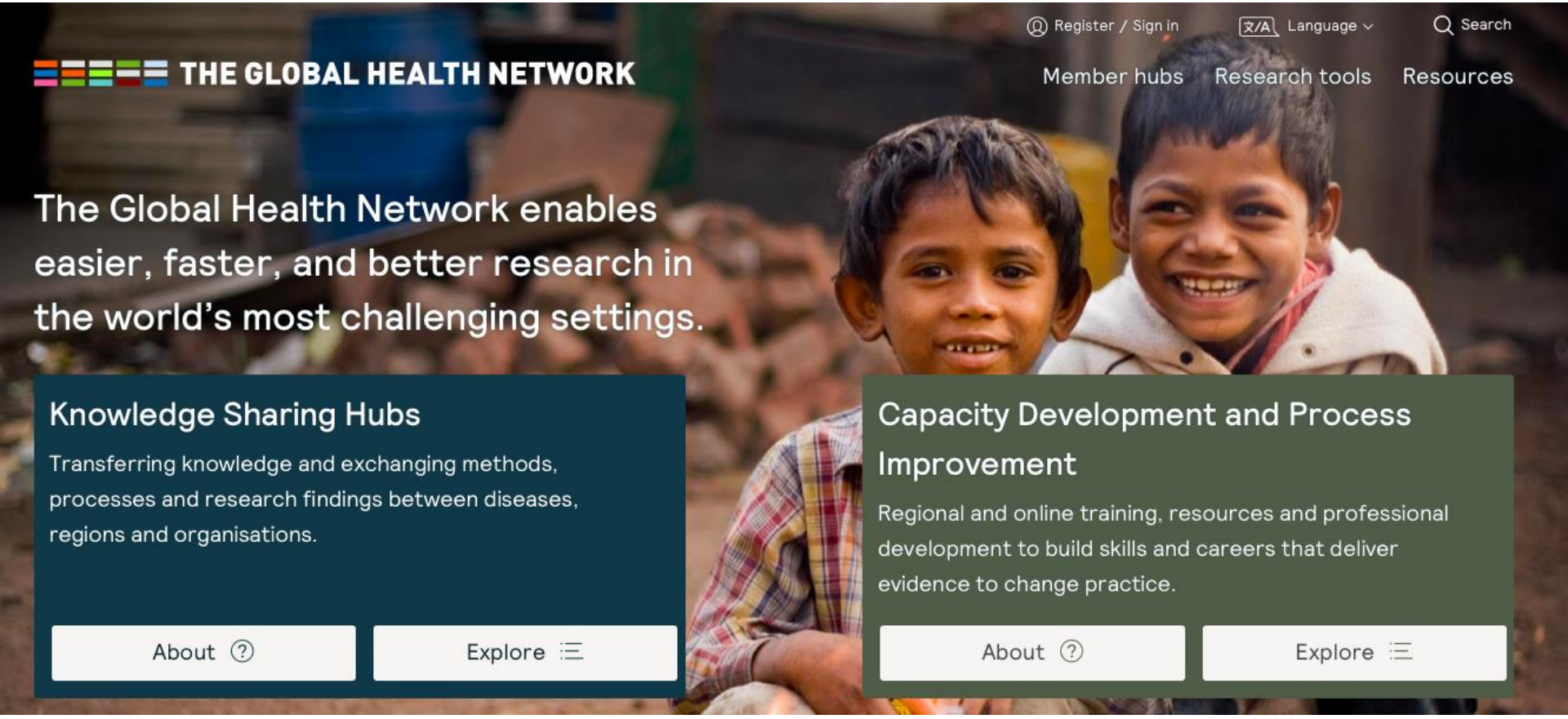
Country	Title
Uganda	The practice of **pilot studies** in informing the conduct of HIV clinical trials in sub Saharan Africa: a review of study protocols
Kenya	Pilot implementation of **Short Message Service for randomisation** in a multisite pragmatic factorial clinical trial in Kenya (PRISMS Study)
Uganda	**Photovoice to explore community members perspectives** regarding health and healthcare challenges in Mukono District, Uganda
Tanzania	Assessment of the **challenges encountered in implementing vaccine clinical trial** methodologies in low income countries
UK/India	**Optimising Informed CONsent** in clinical trials in low- and middle-income settings: feasibility of an adapted QuinteT Recruitment Intervention (QRI) in India (OrION-I)
Thailand	Exploring **barriers to data reuse**
South Africa	**Cultural competence in trial design and conduct**

Many thanks to all involved thus far & the UK Trial Managers' Network for hosting this webinar

Better Research for Better Health

THE GLOBAL HEALTH NETWORK
Enabling research by sharing knowledge

Facilitating health research & delivering research capabilities



Integrated Programmes and Platforms

An online platform and regional programme for knowledge exchange and building lasting capable teams who deliver research excellence

52 ‘communities of practice’ each sharing their know-how between disease areas, roles, regions and organisations

Visited over 28 million times and over 1.3 million ‘how to’ research skills training courses have been taken

Many 100’s of 1000’s of templates, protocols and guidance documents shared downloaded and used, and then re-shared!

This is also a research platform for understanding the barriers and enablers, to improve the process and deliver findings into practice

Impact at a glance

THE GLOBAL HEALTH NETWORK
Enabling research by sharing knowledge

28.8 million

visits to theglobalhealthnetwork.org - 16 million from Africa, Latin America and Asia

265,000+

registered members in our global community, representing a full range of research disciplines and roles in global health research.

1.3 million+

online training modules taken

380,000+

templates, tools and resources downloaded

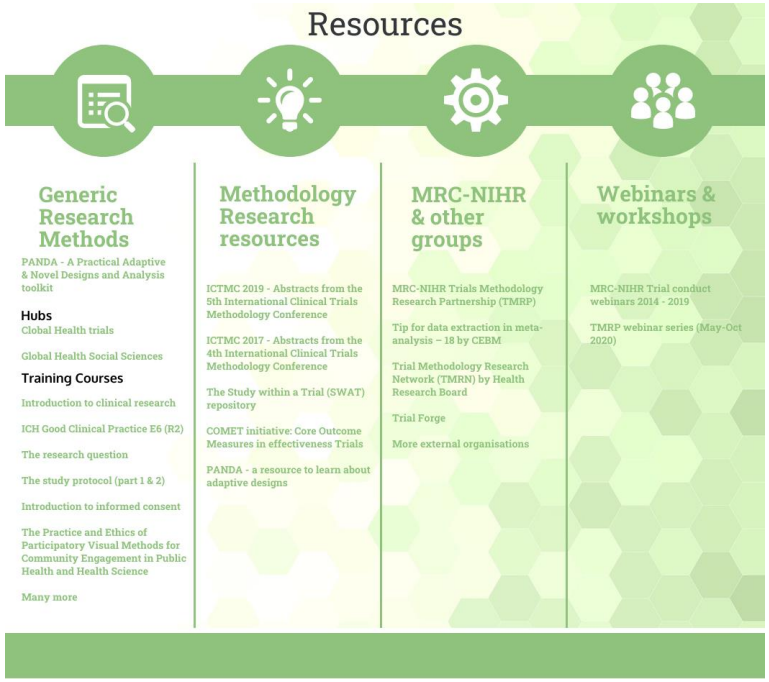
3700

pages of information including 2300 guidance articles and 1300 blog posts

MRC Medical Research Council | NIHR National Institute for Health Research | Trials Methodology TMRP Research Partnership

THE GLOBAL HEALTH NETWORK

Enabling research by sharing knowledge



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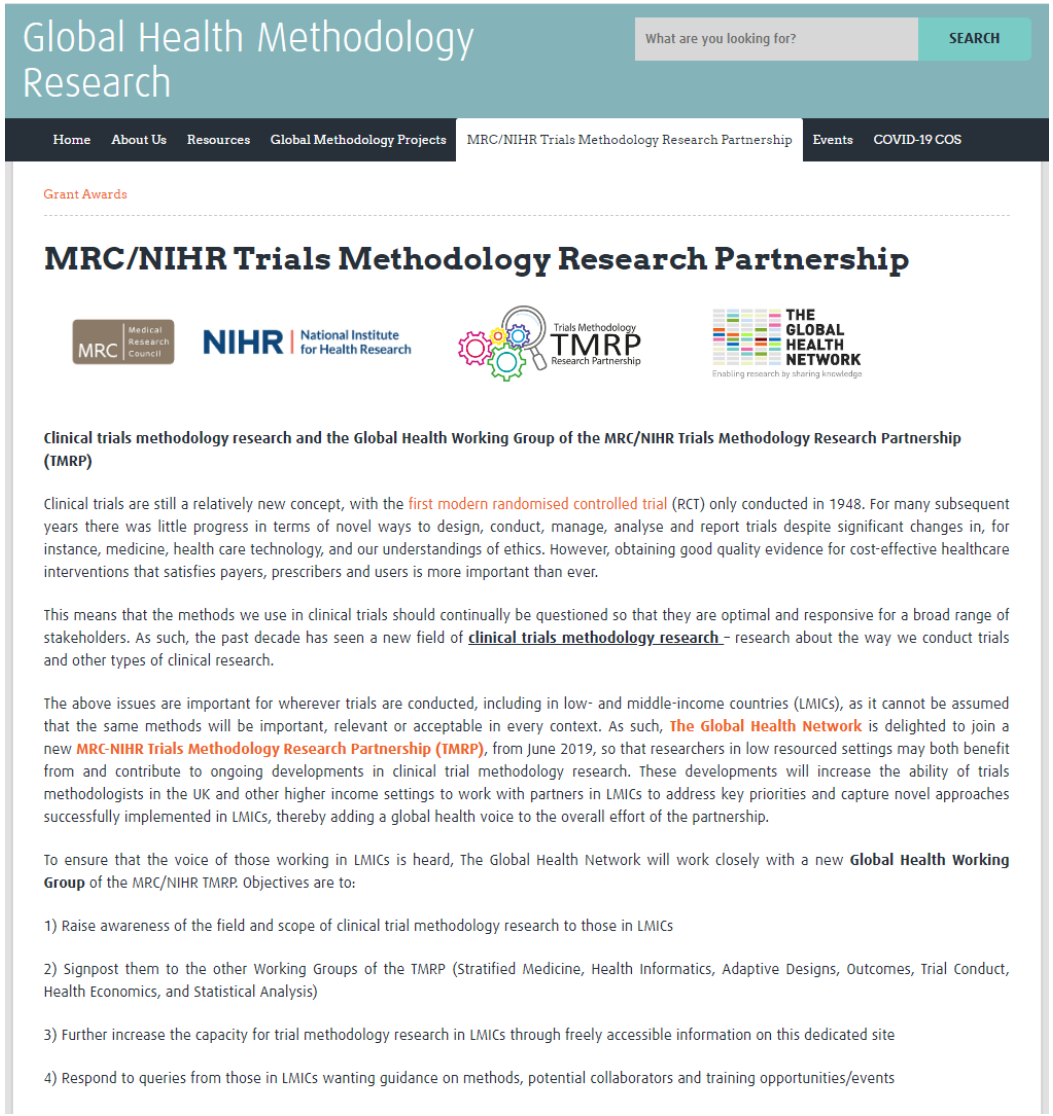


For any other queries about the Global Health Working Group please contact Elizabeth Allen

elizabeth.allen@uct.ac.za

The practice of pilot/feasibility studies in informing the conduct of HIV clinical trials in sub Saharan Africa: a scoping review of study protocols

TMRP Webinar Series

PI: Dr. Sylivia Nalubega, Soroti University, Uganda

CO-Is

Dr. John Bosco Matovu — Ministry of Health, Uganda

Mr. Osuwat Lawrence Obado — Soroti University, Uganda

Assoc. Prof. Dr. Catrin Evans — University of Nottingham, UK

Dr. Brenda Agyeiwaa Poku — University of Nottingham, UK

Background

- **Pilot/feasibility** studies represent a fundamental phase of the research process
  - Are largely a **research methodological requirement**.
  - Play a vital role in the **preliminary planning** of a full size clinical trial
- May include procedures such as the;
  - **pretesting of study tools** on a related sample to the intended study participants
  - affirming the **validity of the sample participants**, and that of **the questions** included in the data collection tools

Background…cont.

- Pilot and feasibility studies are essential in assessing the;
  - feasibility
  - acceptability
  - safety of treatment or interventions
  - recruitment potential
  - randomization and blinding processes
  - and provide estimates for sample size calculation

Background…cont.

- **Advantages**
  - Contribute to the **determination of the most appropriate trial design**
  - Help to **prevent extensions or unintended closure** as a result of failure to recruit sufficient numbers
  - Contribute to **improvements in the quality of research** conducted
  - Contribute to reduction in **waste in research**

Background…cont.

- HIV remains a global health challenge and efforts to curb the epidemic requires new innovations through high quality research including **clinical trials on HIV epidemiology, prevention and treatment**.
- Due to the high incidence and prevalence of HIV in the region, **sub-Saharan Africa remains the hub for large HIV clinical trials** in the world.
- Despite the likely benefits, **the practice of undertaking pilot/feasibility studies as a pre-requisite for conducting HIV clinical trials** in sub Saharan Africa is not well documented.

Problem statement

- Less documentation on how pilot/feasibility studies **inform subsequent larger HIV clinical trials.**
- Likeliness that many pilot/feasibility studies **do not reach their intended goal**.
- This could however, be due to **underreporting** of how the respective pilot/feasibility studies inform the conduct of a subsequent clinical trial.
- If pilot/feasibility studies are not conducted prior to larger HIV clinical trials,
  - The **safety of study participants** could be undermined.
  - There **could be waste** of resources
  - Studies **may not achieve intended outcomes**

Research aim

- We aim to undertake a scoping review of published HIV clinical trial protocols/proposals, to establish **how larger HIV clinical trials have been informed by a prior pilot/feasibility study**.

Research question

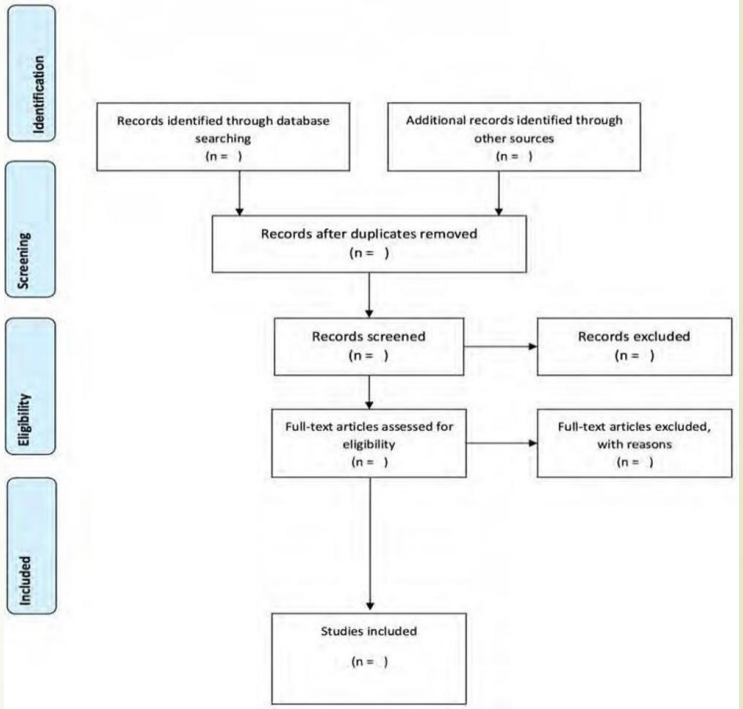
- To what extent do pilot/feasibility studies inform the conduct of HIV clinical trials in sub-Saharan Africa?

Specific questions

- To **estimate the proportion** of HIV clinical trials that are informed by a pilot/feasibility study
- To determine **geographical, clinical trial and funder related factors** that are associated with use of pilot/feasibility studies in informing the conduct of HIV clinical trials

Methodology

- **Scoping review** of protocols/proposals of HIV clinical trials in sub-Saharan Africa.
- Will follow the **JBI approach.**
- Will utilize the **PRISMA-ScR** reporting guideline and checklist.



Methodology…cont.

Inclusion criteria

- **Types of participants/population**
  - Published HIV study protocols/proposals that were **designed for conducting human based HIV clinical trials**
- **Concept**
  - All protocols/proposals that focus on **HIV clinical trials**

- **Context**
  - **sub-Saharan Africa**.
  - **Multiple settings** that include sub-Saharan Africa
  - Protocols/proposals with **unindicated or unclear will be excluded**
- **Types of studies**
  - Published/unpublished protocols/proposals for HIV clinical trials
  - Articles in English language
  - Published in the past 10 years (2011-2020)

Identification of studies

- A three-step search strategy will be utilized.

- Included databases: MEDLINE (OVID), CINAHL, EMBASE, Web of Science, UK Clinical Research Network [UKCRN] Portfolio Database, and African Index Medicus (AIM).
- Gray literature will be searched from Google, Google Scholar, ClinicalTrials.gov, and Cochrane Central Register of Controlled Trials (CENTRAL) databases.

Study selection/screening for eligibility

- All articles will be imported into the **Endnote software** for screening.
- Selection of documents will be performed by **two independent reviewers**.
- Any disagreements that will arise shall be solved by **consensus or by the decision of a third reviewer**.
- Duplicates will be removed before screening
- The selection process will be done at three levels.
  - At **Title** level, at **abstract** and at **full text**
- The review process shall be aligned to the flowchart from the PRISMA-ScR statement

Data extraction

- Data will be **extracted and charted using a structured tool** adapted from the JBI scoping review methodology guideline
- Data to be extracted will include: Author(s), Year of publication, clinical trial phase, year published, country(s) hosting the trial, population, sample size, methodology/methods, intervention (and comparator), duration of the intervention, and funding agency
- We shall finally extract data related to **any indication that the proposed trial was informed by a pilot or feasibility study**.

Scoping Review Details	
Scoping Review title:	
Review objective/s:	
Review question/s:	
Inclusion/Exclusion Criteria	
Population	
Concept	
Context	
Types of evidence source	
Evidence source Details and Characteristics	
Author(s)	
Date (year)	
Article title	
Journal	
Country	
Context (clinical setting, etc…)	
Sample size	
Participants' age	
Participants' sex	
Clinical trial phase	
Methodology	
Intervention/comparator	
Duration of intervention	
Funder(s)	
Details/Results extracted from source of evidence (in relation to the concept of the scoping review)	
Indication that the proposed trial was informed by a pilot or feasibility study	
No indication that the proposed trial was informed by a pilot or feasibility study	

Data analysis/presentation

- Data analysis shall involve **tallying of the numbers** of HIV clinical trial protocols/proposals identified in the last 10 years.
- Data will be **exported into Microsoft excel** for analysis.
- Computation **of proportions of trials** that had a pilot/feasibility study before they commenced shall be done.
- Analysis of how **other variables associate** with the primary outcome will be done.
- Data will be analysed and interpreted using simple **descriptive statistics (**frequencies, means, median, and Standard Deviations)
- **Patterns and trends** (if identified) will be illustrated using figures and/or diagrams, and summarized in **a narrative form**.
- Final conclusions will be drawn from the mapped evidence
- Recommendations for **future research** and provisional recommendations for **practice** may be proposed.

Potential impact

- Cultivating a culture of;
  - reporting of the **outcomes/endpoints** of pilot and feasibility studies
  - accountability to funders and the scientific community
- Influence on the integration of pilot and feasibility studies in HIV clinical trials conduct
- Influence on HIV clinical trial policy and guidelines

Dissemination plans

- Scoping review protocol to be published
- Final scoping review to be published
- Presentation in international conferences


Thank
You

IMPROVING UPTAKE OF CORE OUTCOME SETS IN LOW- AND MIDDLE-INCOME COUNTRIES

Jamlick Karumbi

University of Liverpool, UK

KEMRI Wellcome Trust, Kenya

Background

- When trials assessing the same intervention or condition choose different outcomes to measure or report on it becomes difficult to synthesize results in a systematic review limiting the translation of evidence into practice.
- It also has been shown to lead to selective reporting bias in research.
- Standardizing outcomes and how we measure them is important, enhances research usability and reduce research waste.
- The greater emphasis on the choice of outcomes to measure may also help increase patient centered care when patients are involved in the choice of the outcomes to be measured

What are COS?

- COS are agreed-on minimum standardized outcome sets that should be measured and reported in all clinical trials in a given clinical area.

- They consist of
  - Core Domain Set (this defines what domains should be measured in a trial) and
  - Core Outcome Measurement set (defines the instruments which would be appropriate to measure the domain).

COS development and uptake

- To date, COS have been developed for various conditions or diseases and continue to be developed.
- Over 70% of COS works and participants have been from Europe and North America.
- Virtually no COS that has been initiated from developing countries.
- As of last year about 25% of COS had participants from developing countries

Objectives

An overarching goal is to improve the uptake of COS in LMICs at the various levels of use; i.e. for research, development of clinical guidelines and in routine patient centered clinical practice

To review of the extent of involvement of participants from LMICs and how the approaches differed between COS with
LMICs participants and those with HICs participants

To explore the degree of understanding, involvement and application of COS in LMICs

To assess the adoptability and/or adaptability of existing COS for renal care to LMIC settings

To examine the feasibility developing a COS and tests its implementation using routine data

Methods – Objective 1

Systematic review describing the involvement of participants from LMICs and approaches used.

Guiding questions

- *What is the proportion of COS that have had participants from LMICs?*
- *What were the approaches used in the COS that have had participants from LMICs*

Methodology – Objective 2

Explore the degree of understanding, involvement and application of COS in LMICs through an online survey and a stakeholder's workshop.

Guiding questions

1. *What are experiences of involving participants from LMICs in COS development. [2 surveys]*
    i. An online survey for authors from HIC who had LMICs participants
    ii. An online survey for LMIC participants who have been involved in COS development
2. *In the Kenyan Context, what are Knowledge, Attitude and practice on COS in general? [workshop]*

Methodology – Objective 3

Test the adoptability or adaptability of existing COS to LMIC settings.

Guiding questions

1. *Are COS developed in HIC generalizable to LMICs?*
2. *What are the context issues to consider?*

- *Qualitative methods will be used [Key Informant Interviews, Group interviews and Focused Group Discussions]*

Methodology – Objective 4

Examine the feasibility developing a COS and tests its implementation using routine data

- *Guiding questions*
  1. *Is a rapid COS development process feasible in an LMIC setting in the area of basic newborn care?*
     - Scope definition
     - Systematic review
     - Consensus process - Delphi process, Focused Group Discussions etc
  2. *Can the routine data collection systems be used to assess implementation of COS?*
     - Analysis of data from the Clinical Information Network (CIN) for pediatrics and The East African Renal Registry for Renal

Table 1 Scope of included studies

	HICs n (%) (N=295)	LMICs[#] n (%) (N=75)
Scope of the COS study		
Study aims		
Part of wider trial design	124 (42)	13 (17)
Specific for COS	171 (58)	62 (83)
Intended use of recommendations		
Research	264 (89)	61 (81)
Clinical Practice	0	0
Research and Practice	31 (11)	14 (19)
Population characteristics		
Neonates	4 (1)	1 (1)
Adults	61 (21)	12 (16)
Children	26 (9)	7 (9)
Children and Adults	28 (9)	10 (13)
Not specified*	176 (60)	45 (60)

Public participation			
	Patients	72 (24)	28 (37)
	Carers	26 (9)	17 (23)
	Patient Support group representatives	21 (7)	9 (12)
	Service users	4 (1)	5 (7)
Non-Clinical Research expertise			
	Researchers	55 (19)	21 (28)
	Statisticians	22 (7)	8 (11)
	Epidemiologists	13 (4)	9 (12)
	Academic Representatives	5 (2)	0 (0)
	Methodologists	19 (6)	5 (7)
	Economists	7 (2)	2 (3)
Authorities			
	Regulatory agency representatives	33 (11)	15 (20)
	Government agencies	14 (5)	5 (7)
	Policy makers	10 (3)	7 (9)
	Charities	4 (1)	0 (0)
	Service commissioners	3 (1)	1 (1)

Main methods (not mutually exclusive)	HIC (n) (295)	LMIC (n) (75)
Delphi	83 (28)	47 (63)
Focus group discussion	8 (3)	7 (9)
Nominal Group Techniques	17 (6)	11 (15)
Semi structured discussions	152 (52)	39 (52)
Survey	29 (10)	9 (12)
Literature review	140 (47)	49 (65)
Unstructured group discussions	4 (1)	8 (11)
No methods described	6 (2)	1 (1)

Acknowledgements

Supervisors

University of Liverpool

1. Prof Paula Williamson
2. Prof Bridget Young
3. Dr. Elizabeth Gargon

Kenya Medical Research Institute- Welcome Trust Research

1. Dr. David Gathara

PILOT IMPLEMENTATION OF A MOBILE TEXT MESSAGE-BASED SOLUTION FOR RANDOMIZATION

MERCY CHEPKIRUI

CLINICAL TRIAL DATA MANAGER, KEMRI-WELLCOME TRUST NAIROBI.

KEMRI | Wellcome Trust

SEARCH

THE GLOBAL HEALTH NETWORK
Enabling research by sharing knowledge

OUTLINE

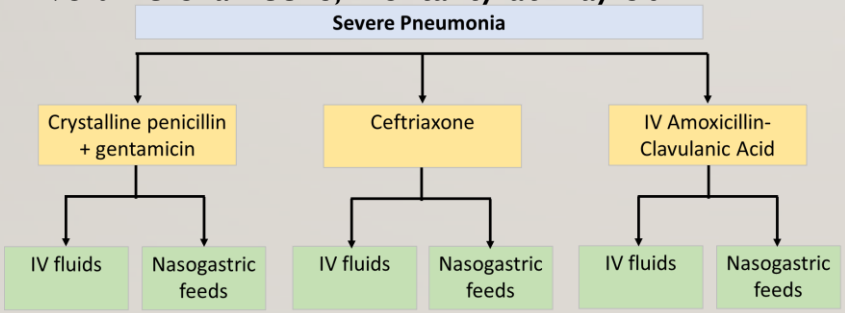
- Background & rationale
- Objectives
- Methodology
- Work plan

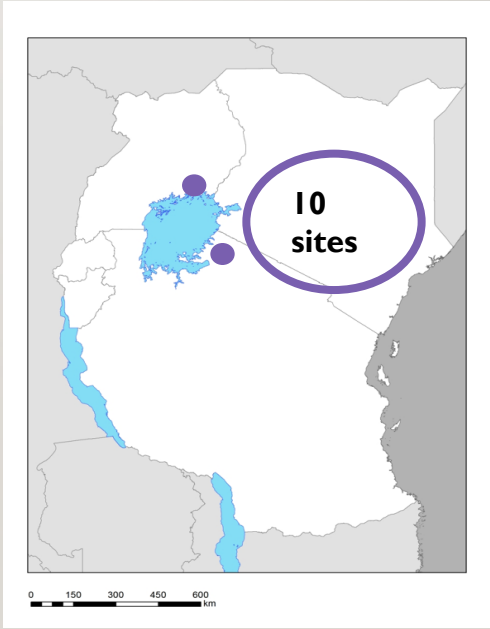
BACKGROUND

- Randomization - the standard method of experimental control
- Randomization involves two steps
  - Generating an unpredictable random sequence,
  - Implementing the sequence in a way that conceals the treatment until the participant have been ***assigned*** the treatment **.**
- Impact of improper randomization
  - Biased estimates of treatment effects
- Traditional methods for concealment
  - The use of sequentially numbered opaque sealed envelopes is prone to manipulation, can get easily damaged during shipping and filling and concealing is time-consuming which is prone to human-error.

SUPPORTIVE CARE AND ANTIBIOTICS FOR SEVERE PNEUMONIA AMONG HOSPITALIZED CHILDREN (SEARCH)

- Randomized pragmatic 3x2 factorial clinical trial
- Sample size: 4392 children in 12 sites
- Primary endpoint: Mortality at Day 5
- Secondary outcomes: length of hospitalisation, time to full volume oral feeds, mortality at Day 30





RATIONALE

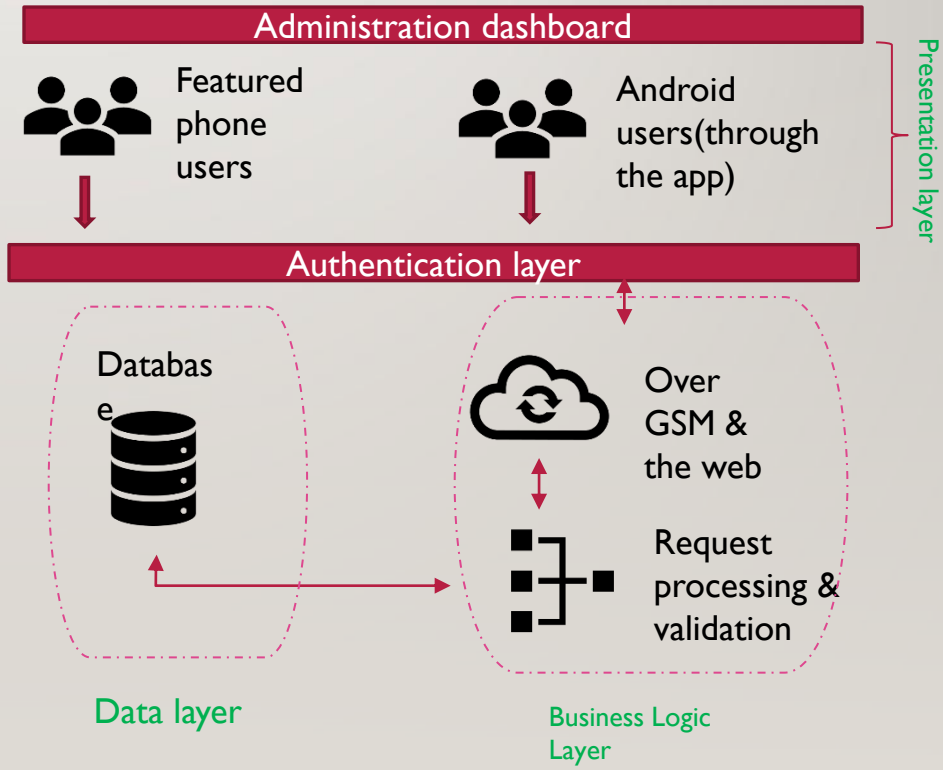
- Centrally-administered web-based/telephone randomization as an option.
- Weak communication infrastructure and poor internet connectivity in low resource settings is a limitation.
- An affordable, auditable, and suitable for low-resource settings is the use of mobile phone-based Short Messaging Service (SMS).
- SMS used in clinical trials
  - To reduce missed appointments (Perron, N. J., 2013)
  - To improve clinic attendance (Chen, Z. W., 2008)
  - As a cost-effective intervention for managing patients with chronic illnesses (Islam, S. M.S., 2019; Finitsis, D. J.,2014; Thakkar,2016; Park, L.G., 2014).
  - SMS reminder trial for malaria case management (Zurovac et al., 2011) to improve adherence to treatment guidelines.
- Rapidly expanding mobile phone technology in developing countries.
- This has the potential to promote equitable improvement in the quality of global health trials by providing a verifiable and convenient method for randomization that works in marginalized settings

OBJECTIVES

- To determine accuracy of SMS randomization against the master randomization list and sealed envelopes (the method being used in the SEARCH trial)
- Estimate response time of SMS delivery for every randomization request across different networks.
- Assess user experience for both approaches.

METHODOLOGY

- Sample size: 200 eligible participants in SEARCH clinical trial.
- 2 study sites in Nairobi
- A pair-wise randomization: A participant will be randomized using 2 methods. The existing envelope method & SMS method.
- Qualitative interviews with the users(Clinical trial team).
- SMS platform development (3-tiers)



WORK PLAN

Period	2020					2021						
	Aug	Sept	Oct	Nov	Dec	Jan	Feb	Mar	April	May	June	July
Developing the SMS platform												
Reporting I												
Clinical trial randomization												
Qualitative interviews												
Reporting II												

THE END

- Thank you

MORU Tropical Health Network

wellcome

Mahidol University

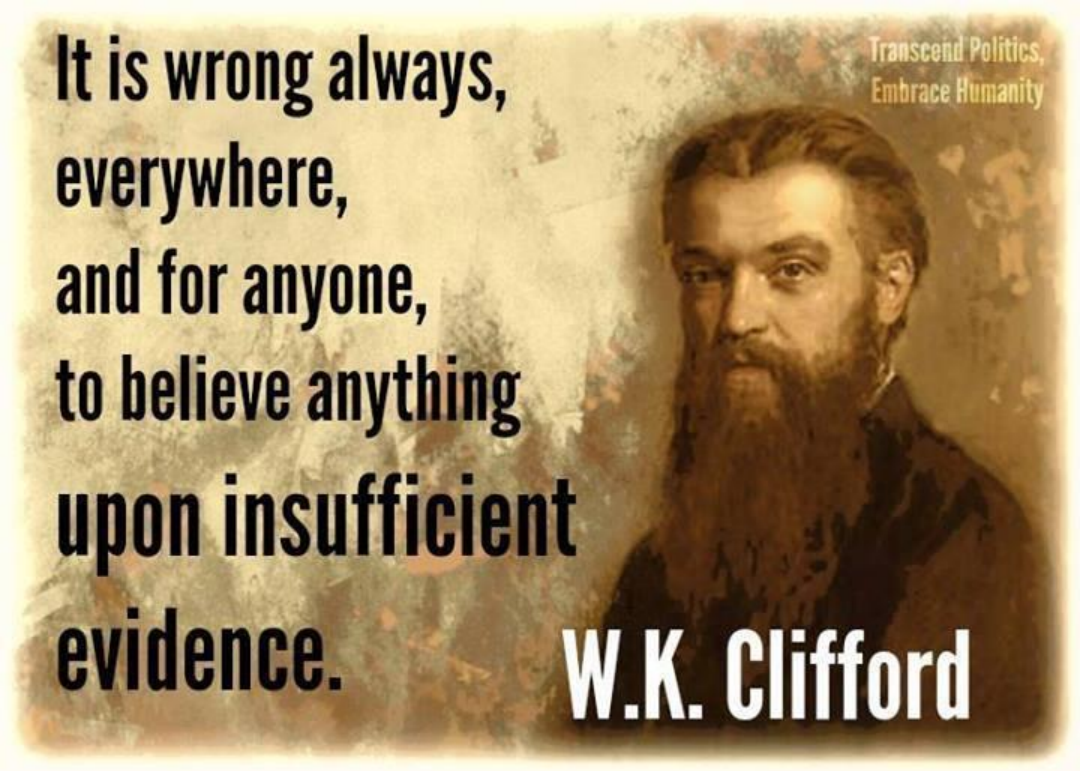
UNIVERSITY OF OXFORD

Promoting reuse of clinical research data

What are the barriers and enablers of data reuse?

Naomi Waithira

Mahidol Oxford Research Unit, Thailand



William Kingdon Clifford *(1845-1879)*
Mathematician and philosopher-introduced geometric algebra

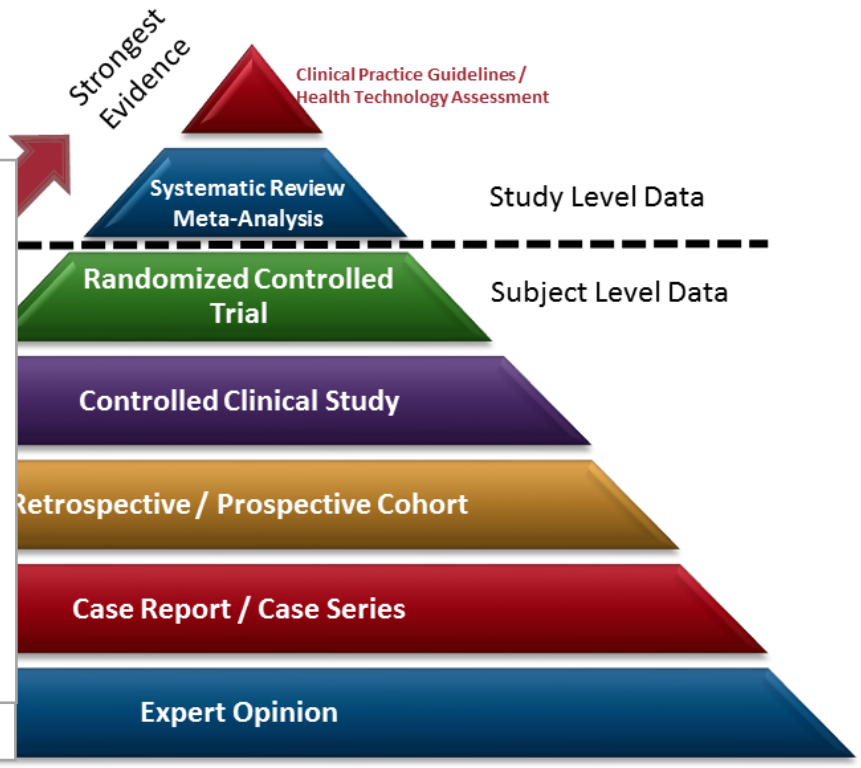
The Evidence Pyramid

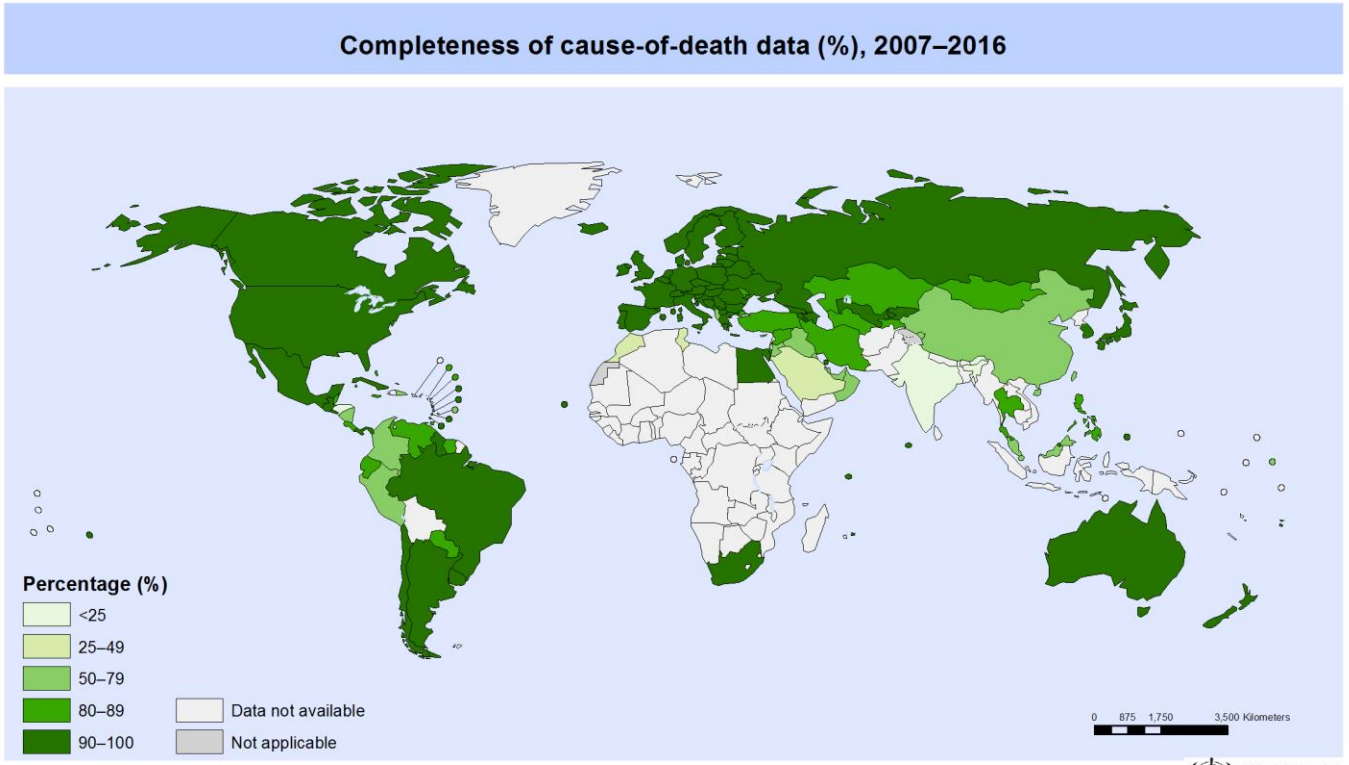
HOW is individual patient-level data from other studies relevant for new studies?

Design:
Baseline/Background data, hypothesis development

Operations:
Determine Cost, Complexity & Feasibility

Analysis: Interpretation of results



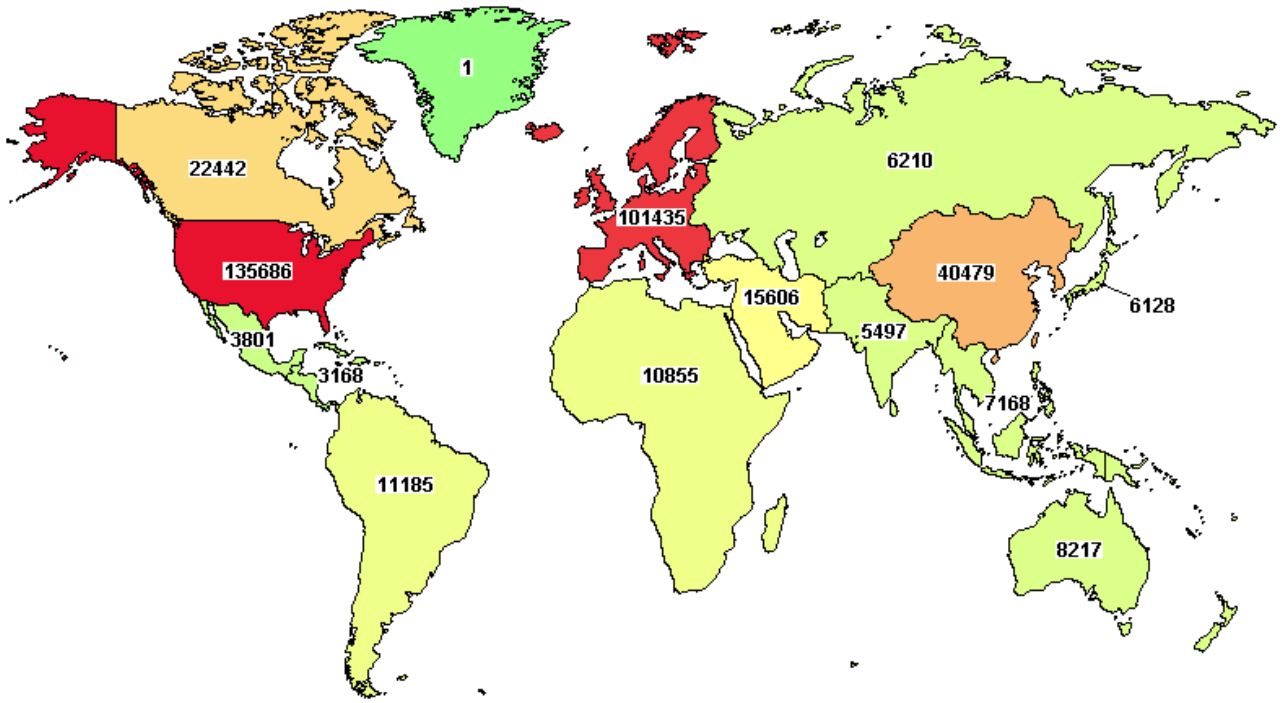


Does the data exist?

Can the data be accessed?

Can the data be used?

Does data exist: **Registered clinical studies**



Source:https://ClinicalTrials.gov

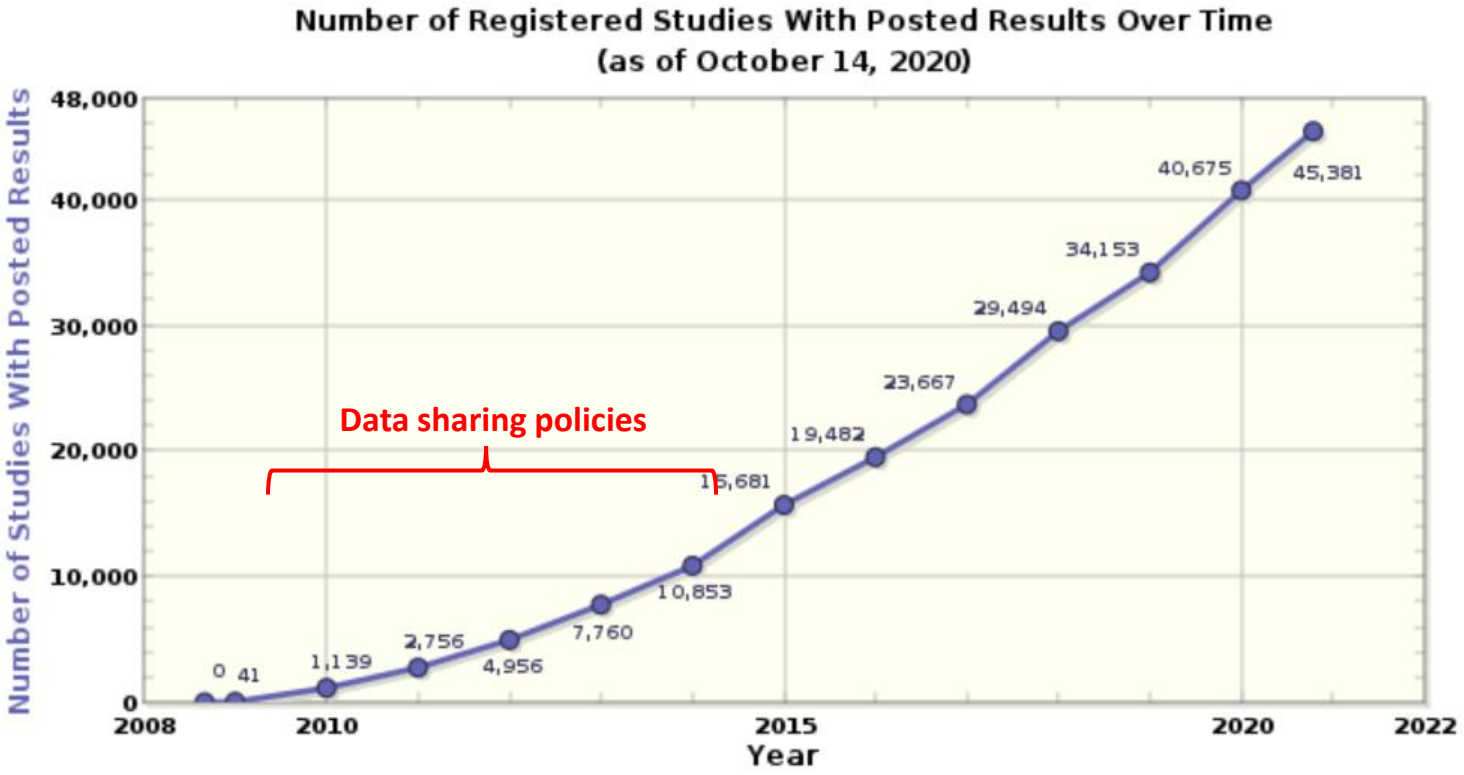
Does the data exist?

Source: https://ClinicalTrials.gov

ICJME: trial registration made a condition for publication (September 2005)

FDAAA: requirements for trial registration

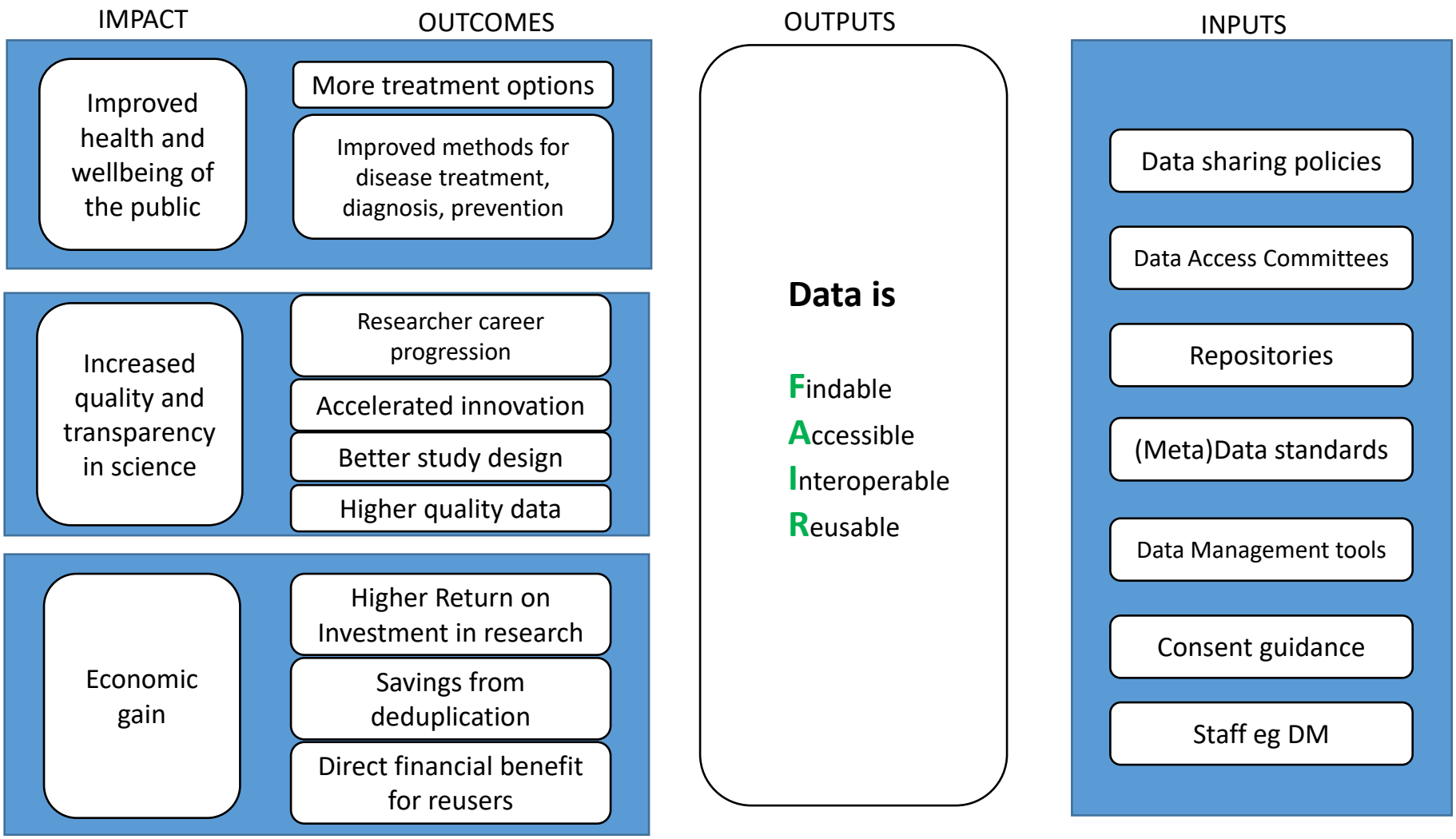
Does the data exist?



Source: https://ClinicalTrials.gov

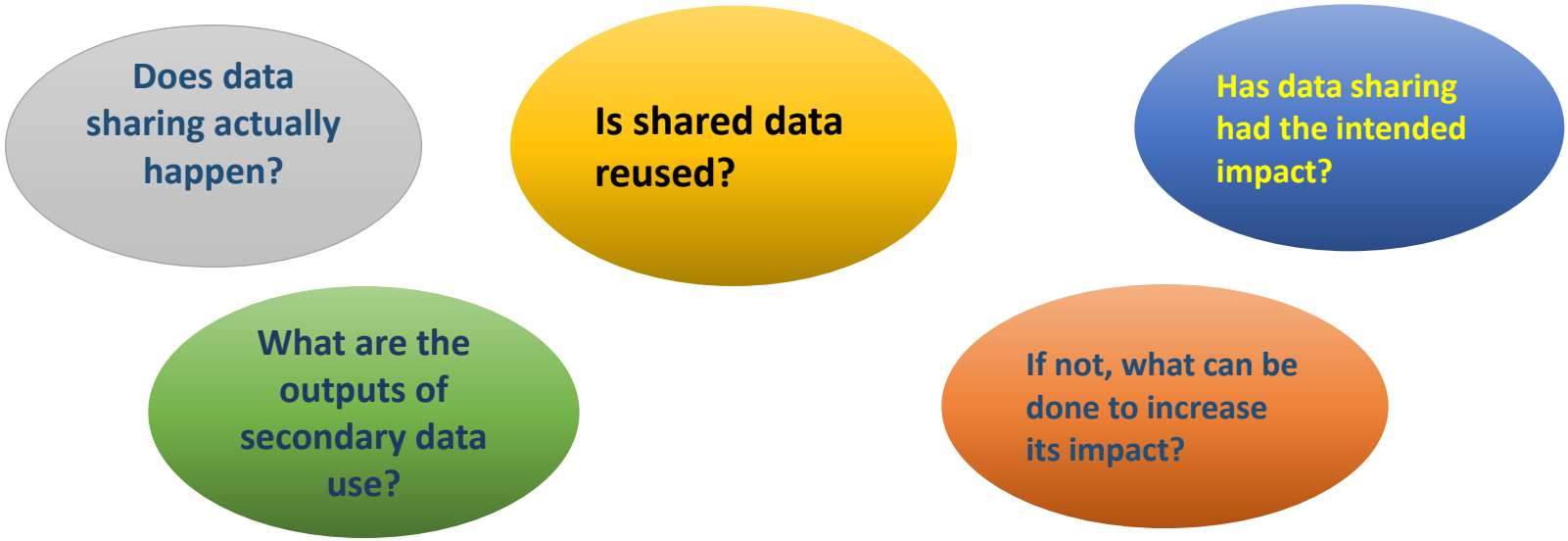
Steady increase in number of studies with posted results over time. Potential increase in number of datasets available

The premise of data sharing


IMPACT
OUTCOMES
OUTPUTS
INPUTS
Improved health and wellbeing of the public
More treatment options
Improved methods for disease treatment, diagnosis, prevention
Increased quality and transparency in science
Researcher career progression
Accelerated innovation
Better study design
Higher quality data
Economic gain
Higher Return on Investment in research
Savings from deduplication
Direct financial benefit for reusers
Data is
Findable
Accessible
Interoperable
Reusable
Data sharing policies
Data Access Committees
Repositories
(Meta)Data standards
Data Management tools
Consent guidance
Staff eg DM

REUSE Study: background

- Thousands of clinical research studies are conducted annually
- Significant investment made to facilitate data collection and ‘sharing’



REUSE study: objectives

Impact of secondary use of clinical research data

Barriers and enablers of secondary use of clinical research data

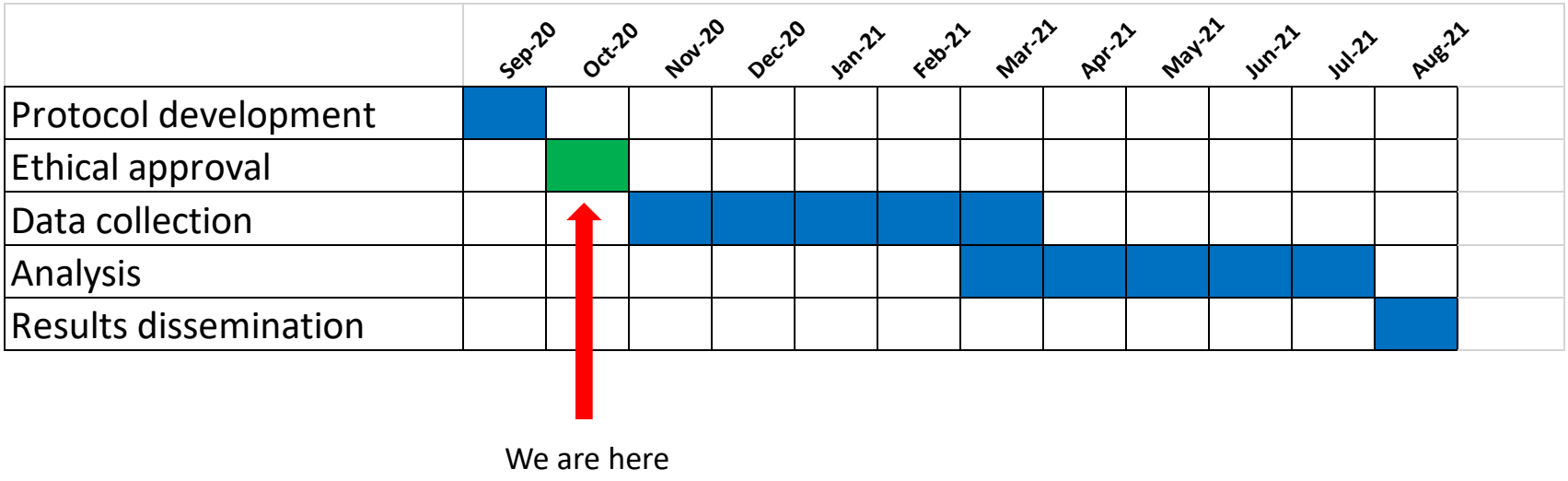
Research questions

1. What outputs are obtained from data reuse?
    i. What benefits have these outputs had for researchers, general public ?
    ii. How has data reuse influenced transparency and quality of research?
2. What difficulties do users experience with data access and reuse?
3. What are the perspectives of the public with regard to use of their data for clinical research purposes.

Methods

- **Online survey**
  - N=200
  - Secondary data users
  - Researchers, Epidemiologists, Statisticians, Artificial Intelligence experts, Regulators, Disease advocacy bodies
- **In-depth interviews**
  - N=20-30
  - similar population as online survey
- **Focus group discussions**
  - 2-3 discussions
  - Public population

Timeline


Sep-20
Oct-20
Nov-20
Dec-20
Jan-21
Feb-21
Mar-21
Apr-21
May-21
Jun-21
Jul-21
Aug-21
Protocol development
Ethical approval
Data collection
Analysis
Results dissemination
We are here

With thanks to **MRC/NIHR Trials Methodology Research Partnership (TMRP)** for funding this work

Thank you.

Mahidol Oxford Tropical Medicine Research Unit

Faculty of Tropical Medicine | Mahidol University | 420/6 Rajvithi Road | Bangkok 10400,Thailand

Thank you to our presenters today.

Please type your questions in the chat box!